phomatous effusions (pleural, pericardial, or ascitic) without a contiguous tumor mass. Primary effusion lymphomas mainly occur in older patients (most in the fourth decade of life) and with more advanced disease than Burkitt-like lymphomas. The patients are usually severely immunosuppressed (T cells <100/mm^3), and most have prior manifestations of AIDS, including opportunistic infections. Morphologically, the tumors resemble B cell immunoblastic and large-cell anaplastic lymphomas. In most patients, disease is limited to body cavities, but occasional cases have involved adjacent organs such as the lung, soft tissues, regional nodes, and bone marrow. KSHV-associated lymphomas have also been identified in the central nervous system and the gastrointestinal tract, in HIV-negative men, and in women. The prognosis is poor, and the majority of patients die within 1 year of diagnosis.

Phenotypically, primary effusion lymphomas express leukocyte common antigen (CD45), but most are negative for other B and T cell–associated antigens including CD20, CD19, and immunoglobulins. The cells have activation antigens including HLA-DR and CD30. Molecular analysis confirms derivation from late differentiating B cells, possibly at the immunoblast, plasmablast, or preplasma cell stage. Herpesvirus particles consisting of 100- to 115-nm capsids with central cores have been identified within neoplastic cells. Most cases in HIV-seropositive individuals are also positive for EBV (type A or B). Unlike most EBV-associated lymphomas, however, there appears to be no involvement of c-*myc*. They also lack *bcl-6* gene rearrangements and *ras* oncogene or *p53* tumor suppressor gene mutations. Cytogenetic studies reveal multiple chromosomal abnormalities. Preliminary data suggest that involvement of two potential oncogenes, one a cellular type D cyclin similar to the PRAD 1 oncogene involved in mantle cell lymphomas, and one homologous to the cellular G protein–coupled receptor (GCR) family of proteins. The virus contains proteins similar to human macrophage inflammatory protein (MIP) chemokines and interleukin-6 (viral IL-6), which may play a role in the pathogenesis and clinical syndrome of multicentric Castleman's disease.

KSHV has been associated with benign lymphoid proliferations from HIV-positive and -negative patients with AILD and multicentric Castleman's disease. KSHV is present in almost all cases of Castleman's disease in patients with AIDS and in approximately half the cases in HIV-seronegative patients. KSHV sequences have also been detected in peripheral blood lymphocytes from patients with Castleman's disease. Multicentric Castleman's disease occurs most often in older patients, predominantly men, and is associated with lymphadenopathy and constitutional symptoms. We have detected KSHV sequences in a child with familial multicentric Castleman's disease, and other children have been seropositive for KSHV. Patients with Castleman's disease may develop secondary malignancies, most commonly Kaposi's sarcoma and non-Hodgkin's lymphoma. In HIV-infected patients with Castleman's disease, there is a strong association between KSHV and sexual transmission, as well as the development of Kaposi's sarcoma.

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Cocaethylene: A Novel Cocaine Homolog

COCAETHYLENE (CE) is a pharmacologically significant homolog of cocaine, formed by transesterification of cocaine with ethanol when the two are ingested concurrently. This reaction is mediated by a hepatic carboxylase which, in the absence of ethanol, catalyzes the production of benzoylecgonine, the major urinary metabolite of cocaine.

As is the case for cocaine, CE binds to the dopamine transporter and inhibits dopamine uptake into synaptosomes. The behavioral pharmacology as well as the psychomotor stimulant effects of CE are similar to those of cocaine, but the toxicity of CE is greater than that of cocaine, and its LD_{50} is much lower. Furthermore, the plasma half-life of CE in humans is longer than that of cocaine, and plasma concentrations of CE often exceed those of cocaine itself. Taken together, these factors make CE a compound of toxicological importance.

Recent work has demonstrated that CE binds with high affinity to human serum alpha-1 acid glycoprotein (orosomucoid) and with low affinity to serum albumin. Human brain, heart, liver, and placenta also bind both cocaine and CE.

Both cocaine and CE can be quantitated simultaneously in plasma and urine by high-pressure liquid chromatography. Thin-layer chromatography of urine is useful for the qualitative detection of cocaine and CE if a solvent system consisting of hexane (65 ml):toluene (20 ml):diethylamine (5 ml) is used. Both compounds can be readily visualized as reddish-brown spots after the plate is sprayed with iodoplatinate (cocaine, R_f 0.44; CE, R_f 0.51). Furthermore, both are metabolized to benzoylec-

gonine, which can be easily detected by qualitative immunoassay of the urine.

While not likely to be encountered clinically, the isopropyl and propyl homologs of cocaine (cocaisopropylene and cocapropylene) have also been described, and their formation has been demonstrated by incubation of human liver homogenates with isopropanol and *n*-propanol, respectively. These compounds, if present in urine, can be detected by thin-layer chromatography.

Detection of CE and other cocaine homologs is clinically important since their presence may help explain persistence of drug effects after the parent drug has dissipated.

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